

Mild bronchial asthma: The present and the future

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Abstract

© 2018 Medical Education. All rights reserved. Mild asthma is characterized by infrequent and slight clinical manifestations and, therefore, is paid lack of attention both from patients and physicians. Physicians tend to underestimate risk of severe exacerbations including asthmatic status in patients with mild asthma. Patients with mild asthma are often poorly adherent to treatment. Also, certain difficulties are related to timely and correct diagnosis and the choice of the optimal treatment by primary care physicians who are first physicians encountering such patients. The paradoxus of asthma and use of short-acting β 2-agonists (SABA) to treat chronic airway inflammation lead to excessive dependence on rescue inhalers and insufficient adherence to maintenance anti-inflammatory therapy. This could trigger acute exacerbations and even fatal outcomes in patients with mild asthma. Therefore, SABA monotherapy has to be limited. Easy-to-use questionnaires, algorithms and treatment protocols accessible for primary care physicians could improve detection of mild asthma. Favorable results of clinical trials on as-needed use of budesonide/formoterol Turbuhaler® could change the management paradigm for mild asthma regarding risk of exacerbations, control of asthma symptoms, airway inflammation, and cost-efficacy.

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Keywords

As-needed use of inhaled corticosteroid/long-acting β 2-agonist combination,
Budesonide/formoterol, Inhaled corticosteroids, Mild asthma, Short-acting β 2-agonists

References

- [1] Dusser D., Montani D., Chanez P. et al. Mild asthma: an expert review on epidemiology, clinical characteristics and treatment recommendations. *Allergy*. 2007; 62 (6): 591-604. DOI: 10.1111/j.1398-9995.2007.01394.x.
- [2] 2. Arkhipov V.V., Grigor'eva E.V., Gavrishina E.V. Control of bronchial asthma in Russia: results of the NIKA multi-center observational study. *Pul'monologiya*. 2011; (6): 87-93. DOI: 10.18093/0869-0189-2011-0-6-87-93 (in Russian).
- [3] Kulbaisov A.M., Polumordvintseva T.V., Zhestkov A.V. Pharmacotherapy of bronchial asthma: problems and possible solutions. 2017. *Vestnik sovremennoy klinicheskoy medi-tsiny*. 2017; 10 (3): 18-23. DOI: 10.20969/VSKM.2017. 10(3).18-23 (in Russian).
- [4] Leshchenko I.V., Chirkov V.I., Livshits A.A. Epidemiology of bronchial asthma in a large industrial region. *Tera-pevticheskiy arkhiv*. 1998; 70 (12): 41-43 (in Russian).
- [5] Bo D., Small M. Disease burden of mild asthma: findings from a cross-sectional real-world survey. *Adv. Ther.* 2017; 34 (5): 1109-1127. DOI: 10.1007/s12325-017-0520-0.
- [6] Royal College of Physicians. Why asthma still kills: the National Review of Asthma Deaths (NRAD) Confidential Enquiry report. London: RCP; 2014. Available at: <https://www.rcplondon.ac.uk/projects/outputs/why-asthm-still-kills> [Accessed 09 January, 2018].

- [7] Price D., Fletcher M., van der Molen T. Asthma control and management in 8,000 European patients: the REcognise Asthma and Link to Symptoms and Experience (REALISE) survey. *NPJ Prim. Care Respir. Med.* 2014; 24: 14009. DOI: 10.1038/npjpcrm.2014.9.
- [8] Sadatsafavi M., Lynd L., Marra C. et al. Direct health care costs associated with asthma in British Columbia. *Can. Respir. J.* 2010; 17 (2): 74-80. DOI: 10.1155/2010/361071.
- [9] Nunes C., Pereira A.M., Morais-Almeida M. Asthma costs and social impact. *Asthma Res. Pract.* 2017; 3: 1. DOI: 10.1186/s40733-016-0029-3.
- [10] Russian Respiratory Society, Clinical Guidelines for Bronchial Asthma. 2016. Available at: <http://spulmo.ru/obrazovatelnye-resursy/federalnye-klinicheskie-rekomendatsii/> (in Russian).
- [11] Jose B.P., Camargos P.A., Cruz Filho A.A., Correa R.A. Diagnostic accuracy of respiratory diseases in primary health units. *Rev. Assoc. Med. Bras.* 2014; 60: 599-612.
- [12] Magnoni M.S., Caminati M., Senna G. et al. Asthma under/misdiagnosis in primary care setting: an observational community-based study in Italy. *Clin. Mol. Allergy.* 2015; 13: 26. DOI: 10.1186/s12948-015-002-x.
- [13] National Asthma Education and Prevention Program: Expert panel report 3: Guidelines for the diagnosis and management of asthma. Full Report 2007. National Heart, Lung, and Blood Institute; 2007.
- [14] Gillis R.M.E., van Litsenburg W., van Balkom R.H. et al. The contribution of an asthma diagnostic consultation service in obtaining an accurate asthma diagnosis for primary care patients: results of a real-life study. *NPJ Prim. Care Respir. Med.* 2017; 27 (1): 35. DOI: 10.1038/s41533-017-0027-9.
- [15] From the Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma (GINA), 2017. Available at: <http://www.ginasthma.org/> [Accessed 09 January, 2018].
- [16] Aisanov Z., Avdeev S., Arkhipov V. et al. Russian guidelines for the management of COPD: algorithm of pharmacologic treatment. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2018; 13: 183-187. DOI: 10.2147/COPD.S153770.
- [17] Loymans R.J., Gemperli A., Cohen J. et al. Comparative effectiveness of long term drug treatment strategies to prevent asthma exacerbations: network meta-analysis. *Br. Med. J.* 2014; 348: g3009. DOI: 10.1136/bmj.g3009.
- [18] Emel'yanov A.V., Goryachkina L.A., Astaf'eva N.G. et al. Allergic rhinitis and bronchial asthma in real clinical practice: results of Russian multi-center study. *Rossiyskiy allergo-logicheskiy zhurnal.* 2012; (1): 29-36 (in Russian).
- [19] Ebmeier S., Thayabaran D., Braithwaite I. et al. Trends in international asthma mortality: analysis of data from the WHO Mortality Database from 46 countries (1993-2012). *Lancet.* 2017; 390 (10098): 935-945. DOI: 10.1016/S0140-6736(17)31448-4.
- [20] Sears M.R., Taylor D.R., Print C.G. et al. Regular inhaled beta-agonist treatment in bronchial asthma. *Lancet.* 1990; 336 (8728): 1391-1396. DOI: 10.1016/0140-6736(90)93098-A.
- [21] Gauvreau G.M., Jordana M., Watson R.M. et al. Effect of regular inhaled albuterol on allergen-induced late responses and sputum eosinophils in asthmatic subjects. *Am. J. Respir. Crit. Care Med.* 1997; 156 (6): 1738-1745. DOI: 10.1164/ajrccm.156.6.96-08042.
- [22] Aldridge R.E., Hancox R.J., Robin Taylor D. et al. Effects of terbutaline and budesonide on sputum cells and bronchial hyperresponsiveness in asthma. *Am. J. Respir. Crit. Care Med.* 2000; 161 (5): 1459-1464. DOI: 10.1164/ajrccm.161.5.9906052.
- [23] Cockcroft D.W., Swystun V.A., Bhagat R. Interaction of inhaled beta 2 agonist and inhaled corticosteroid on airway responsiveness to allergen and methacholine. *Am. J. Respir. Crit. Care Med.* 1995; 152 (5, Pt 1):1485-1489. DOI: 10.1164/ajrccm.152.5.7582281.
- [24] Cockcroft D.W., O'Byrne P.M., Swystun V.A., Bhagat R. Regular use of inhaled albuterol and the allergen-induced late asthmatic response. *J. Allergy Clin. Immunol.* 1995; 96 (1): 44-49. DOI: 10.1016/S0091-6749(95)70031-5.
- [25] Hancox R.J., Aldridge R.E., Cowan J.O. et al. Tolerance to beta-agonists during acute bronchoconstriction. *Eur. Respir. J.* 1999; 14 (2): 283-287.
- [26] Haahtela T., Tuomisto L.E., Pietinalho A. et al. A 10 year asthma programme in Finland: major change for the better. *Thorax.* 2006; 61 (8): 663-670. DOI: 10.1136/thx.2005.055699.
- [27] Pauwels R.A., Pedersen S., Busse W.W. et al. Early intervention with budesonide in mild persistent asthma: a randomised, double-blind trial. *Lancet.* 2003; 361 (9363): 1071-1076. DOI: 10.1016/S0140-6736(03)12891-7.
- [28] Reddel H.K., Busse W.W., Pedersen S. et al. Should recommendations about starting inhaled corticosteroid treatment for mild asthma be based on symptom frequency: a post-hoc efficacy analysis of the START study. *Lancet.* 2017; 389 (10065): 157-166. DOI: 10.1016/S0140-6736(16)31399-X.
- [29] Suissa S., Ernst P., Benayoun S. et al. Low-dose inhaled corticosteroids and the prevention of death from asthma. *N. Engl. J. Med.* 2000; 343 (5): 332-336. DOI: 10.1056/NEJM200008033430504.

- [30] Gauvreau G.M., Doctor J., Watson R.M. et al. Effects of inhaled budesonide on allergen-induced airway responses and airway inflammation. *Am. J. Respir. Crit. Care Med.* 1996; 154 (5): 1267-1271. DOI: 10.1164/ajrccm.154.5. 8912734.
- [31] Gauvreau G.M., Boulet L.P., Postma D.S. et al. Effect of low-dose ciclesonide on allergen-induced responses in subjects with mild allergic asthma. *J. Allergy Clin. Immunol.* 2005; 116 (2): 285-289. DOI: 10.1016/j.jaci.2005.05.021.
- [32] Lange P., Scharling H., Ulrik C.S., Vestbo J. Inhaled corticosteroids and decline of lung function in community residents with asthma. *Thorax.* 2006; 61 (2): 100-104. DOI: 10.1136/thx.2004.037978.
- [33] Barnes C.B., Ulrik C.S. Asthma and adherence to inhaled corticosteroids: current status and future perspectives. *Respir. Care.* 2015; 60 (3): 455-468. DOI: 10.4187/respcare.03200.
- [34] Krishnan J.A., Rieker K.A., McCoy J.V. et al. Corticosteroid use after hospital discharge among high-risk adults with asthma. *Am. J. Respir. Crit. Care Med.* 2004; 170 (12): 1281-1285. DOI: 10.1164/rccm.200403-409OC.
- [35] Piecoro L.T., Potoski M., Talbert J.C., Doherty D.E. Asthma prevalence, cost, and adherence with expert guidelines on the utilization of health care services and costs in a state Medicaid population. *Health Serv. Res.* 2001; 36 (2): 357-371.
- [36] O'Byrne P.M., Pedersen S., Lamm C.J. et al. Severe exacerbations and decline in lung function in asthma. *Am. J. Respir. Crit. Care Med.* 2009; 179 (1): 19-24. DOI: 10.1164/ rccm.200807-1126OC.
- [37] O'Byrne P.M., Pedersen S., Schatz M. et al. The poorly explored impact of uncontrolled asthma. *Chest.* 2013; 143 (2): 511-523. DOI: 10.1378/chest.12-0412.
- [38] Murphy V.E., Clifton V.L., Gibson P.G. Asthma exacerbations during pregnancy: incidence and association with adverse pregnancy outcomes. *Thorax.* 2006; 61 (2): 169-176. DOI: 10.1136/thx.2005.049718.
- [39] Boulay M.E., Boulet L.P. Discordance between asthma control clinical, physiological and inflammatory parameters in mild asthma. *Respir. Med.* 2013; 107 (4): 511-518. DOI: 10.1016/j.rmed.2012.12.015.
- [40] O'Byrne P.M., Jenkins C., Bateman E.D. The paradoxes of asthma management: time for a new approach? *Eur. Respir. J.* 2017; 50 (3): 1701103. DOI: 10.1183/13993003. 01103-2017.
- [41] Busse W.W., Pedersen S., Pauwels R.A. et al. The Inhaled Steroid Treatment As Regular Therapy in Early Asthma (START) study 5-year follow-up: Effectiveness of early intervention with budesonide in mild persistent asthma. *J. Allergy Clin. Immunol.* 2008; 121 (5): 1167-1174. DOI: 10.1016/j.jaci.2008.02.029.
- [42] Lacasse Y., Archibald H., Ernst P., Boulet L.P. Patterns and determinants of compliance with inhaled steroids in adults with asthma. *Can. Respir. J.* 2005; 12 (4): 211-217.
- [43] Papi A., Canonica G.W., Maestrelli P. et al. Rescue use of beclomethasone and albuterol in as a single inhaler for mild asthma. *N. Engl. J. Med.* 2007; 356 (20): 2040-2052. DOI: 10.1056/NEJMoa063861.
- [44] Avdeev S.N., Aisanov Z.R., Arkhipov V.V. et al. Principles of treatment choice in patients with mild bronchial asthma. *Prakticheskaya pul'monologiya.* 2017; (1): 82-92 (in Russian).
- [45] Rabe K.F., Atienza T., Magyar P. et al. Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations: a randomised controlled, double-blind study. *Lancet.* 2006; 368 (9537): 744-753. DOI: 10.1016/ S0140-6736(06)69284-2.
- [46] Patel M., Pilcher J., Pritchard A. et al. Efficacy and safety of maintenance and reliever combination budesonide-formoterol inhaler in patients with asthma at risk of severe exacerbations: a randomised controlled trial. *Lancet Respir. Med.* 2013; 1 (1): 32-42. DOI: 10.1016/S2213-2600(13)70007-9.
- [47] Jorup C., Lythgoe D., Bisgaard H. Budesonide/formoterol maintenance and reliever therapy in adolescent patients with asthma. *Eur. Respir. J.* 2018; 51 (1): 1701688. DOI: 10.1183/ 13993003.01688-2017.
- [48] Bisgaard H., Le Roux P., Bjamer D. et al. Budesonide/formoterol maintenance plus reliever therapy: a new strategy in pediatric asthma. *Chest.* 2006; 130 (6): 1733-1743. DOI: 10.1378/chest.130.6.1733.
- [49] Haahtela T., Tamminen K., Malmberg L.P. et al. Formoterol as needed with or without budesonide in patients with intermittent asthma and raised NO levels in exhaled air: a SOMA study. *Eur. Respir. J.* 2006; 28 (4): 748-755. DOI: 10.1183/09031936.06.00128005.
- [50] Papi A., Marku B., Scichilone N. et al. Regular versus as-needed budesonide and formoterol combination treatment for moderate asthma: a non-inferiority, randomised, double-blind clinical trial. *Lancet Respir. Med.* 2015; 3 (2): 109-119. DOI: 10.1016/S2213-2600(14)70266-8.
- [51] O'Byrne P.M., FitzGerald J.M., Zhong N. et al. The SYGMA programme of phase 3 trials to evaluate the efficacy and safety of budesonide/formoterol given 'as needed' in mild asthma: study protocols for two randomised controlled trials. *Trials.* 2017; 18 (1): 12-25. DOI: 10.1186/s13063-016-1731-4.
- [52] Beasley R., Pavord I., Papi A. et al. Description of a randomised controlled trial of inhaled corticosteroid/fast-onset LABA reliever therapy in mild asthma. *Eur. Respir. J.* 2016; 47 (3): 981-984. DOI: 10.1183/13993003.01692-2015.
- [53] Fingleton J., Hardy J., Baggott C. et al. Description of the protocol for the PRACTICAL study: a randomised controlled trial of the efficacy and safety of ICS/LABA reliever therapy in asthma. *BMJ Open Respir. Res.* 2017; 4 (1): e000217. DOI: 10.1136/bmjresp-2017-000217.